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☐ 1. Document ID: US 20020071839 A1 WO 200168132 A1 AU 200143617 A  
 L3: Entry 1 of 1 File: DWPI Jun 13, 2002

DERWENT-ACC-NO: 2001-589995

DERWENT-WEEK: 200243

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TITLE: Down-modulating the immune response to an intestinal allograft for reducing cytotoxic T-cell responses involves administration of a combination of at least two antibodies which binds to at least two different B7 molecules

INVENTOR: COLLINS, M; NEWELL, K

PRIORITY-DATA: 2000US-189165P (March 14, 2000), 2001US-0805801 (March 13, 2001)

## PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 20020071839 A1	June 13, 2002		000	A61K039/395
WO 200168132 A1	September 20, 2001	E	056	A61K039/395
AU 200143617 A	September 24, 2001		000	A61K039/395

INT-CL (IPC): A61 K 31/445; A61 K 31/4745; A61 K 39/395; A61 P 37/06; A61 K 39/395;  
 A61 K 31:445

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC	Draw Desc	Image
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Term	Documents
B7-1.DWPI,EPAB,JPAB.	44
B7-1S	0
B7-2.DWPI,EPAB,JPAB.	42
B7-2S	0
B7.DWPI,EPAB,JPAB.	1482
B7S	0
CD80.DWPI,EPAB,JPAB.	50
CD80S	0
CD86.DWPI,EPAB,JPAB.	63
CD86S	0
((('B7-1' OR 'B7-2' OR B7 OR CD80 OR CD86)SAME (ANTIBOD\$) AND (GRAFT\$ OR TRANSPLANT\$) SAME (INTESTINES\$)).JPAB,EPAB,DWPI.	1

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1/3/2 (Item 2 from file: 654)  
DIALOG(R)File 654:US PAT.FULL.  
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4744812

Utility

Non-myeloablative tolerogenic treatment

Inventor: Slavin, Shimon, Jerusalem, IL

Prigozhina, Tatyana, Rehovot, IL

Assignee: Hadasit Medical Research Services and Development Ltd. (03),  
Jerusalem, IL

Examiner: Schwartzman, Robert A. (Art Unit: 162)

Assistant Examiner: Beckerleg, Anne Marie

Law Firm: Townsend and Townsend and Crew LLP

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 6447767	A	20020910	US 2000506082	20000216
CIP	Pending			US 98222011	19981231
CIP	Abandoned			US 97862550	19970523
Priority				US 2000506082	20000216
				US 98222011	19981231
				US 97862550	19970523

1/3/7 (Item 7 from file: 654)  
DIALOG(R)File 654:US PAT.FULL.  
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4665984

Derwent Accession: 1995-382847

Utility

C/ Methods for inducing T cell unresponsiveness to donor tissue or organ in  
a recipient with gp39 antagonists

Inventor: Noelle, Randolph J., Cornish, NH

Durie, Fiona H., Seattle, WA

Assignee: University of Massachusetts Medical Center (02), Worcester, MA

Trustees of Dartmouth College (02), Hanover, NH

Dartmouth College Trustees of

Massachusetts, University of Medical Center (Code: 05682 22237)

Examiner: Gambel, Phillip (Art Unit: 164)

Combined Principal Attorneys: Teskin, Robin L.

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 6375950	A	20020423	US 99227081	19990105
Division	US 5902585	A		US 97906332	19970805
Division	US 5683693	A		US 94234987	19940427
Priority				US 99227081	19990105
				US 97906332	19970805
				US 94234987	19940427

1/3/8 (Item 8 from file: 654)  
DIALOG(R)File 654:US PAT.FULL.  
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4625509

Derwent Accession: 1999-327397

# Utility

C/ Method of suppressing an immune response to a transplanted organ or tissue by administering an OX-2 protein; SUPPRESSION AN IMMUNE RESPONSE TO A TRANSPLANTED ORGANS OR TISSUES IN ANIMALS

Inventor: Gorczynski, Reginald M., Willowdale, CA

Assignee: Transplantation Technologies Inc. (03), Toronto, CA

Transplantation Technologies Inc CA (Code: 59636)

Examiner: Gambel, Phillip (Art Unit: 164)

Assistant Examiner: Roark, Jessica H.

Law Firm: Bereskin & Parr

Combined Principal Attorneys: Gravelle, Micheline

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 6338851	A	20020115	US 2000570367	20000505
Continuation	Pending			WO 98CA1038	19981106
Priority				US 2000570367	20000505
				WO 98CA1038	19981106
Provisional				US 60-64764	19971107

1/3/9 (Item 9 from file: 654)

DIALOG(R)File 654:US PAT.FULL.

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4561268 \*\*IMAGE Available

Derwent Accession: 1999-479311

## Utility

REASSIGNED

C/ Costimulatory blockade and mixed chimerism in allo-transplantation; PREVENTING GRAFT REJECTION IN HUMANS; ADMINISTER HUMAN A MODULATOR OF LIGAND ACTIVITY, INSERT HEMATOPOIETIC STEM CELLS AND GRAFT INTO HUMAN, MONITOR RESPONSE TO GRAFTS

Inventor: Sayegh, Mohamed, Westwood, MA

Sykes, Megan, Charlestown, MA

Assignee: The General Hospital Corporation (02), Charlestown, MA

General Hospital Corp The (Code: 10301)

Examiner: Park, Hankyel T. (Art Unit: 168)

Law Firm: Hale and Dorr LLP

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 6280957	A	20010828	US 99245614	19990204
Priority				US 99245614	19990204
Provisional				US 60-73864	19980204

1/3/13 (Item 13 from file: 654)

DIALOG(R)File 654:US PAT.FULL.

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4317430

Derwent Accession: 1995-022455

## Utility

CERTIFICATE OF CORRECTION

C/ Surrogate tolerogenesis for the development of tolerance to xenografts; PRODUCING WITHIN A SURROGATE, ORGANS FOR TRANSPLANT THAT ARE REPOPULATED WITH CELLS FROM THE ORGAN GRAFT RECIPIENT, LESSENING THE ANTIGEN DIFFERENCE AND THEREFORE THE RISK OF REJECTION.

Inventor: Beschorner, William E., Baldwin, MD

Assignee: Ximerex, Inc. (02), Omaha, NE

Ximerex Inc (Code: 53281)

Examiner: Crouch, Deborah (Art Unit: 162)  
Assistant Examiner: Beckerleg, Anne Marie S.  
Law Firm: Banner & Witcoff, Ltd.

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 6060049	A	20000509	US 95295899	19950606
Continuation	Pending			US 9365370	19930524
PCT	WO 9427622		19931208	WO 94US5844	19940524
			371:19950606		
			102e:19950606		
Priority				US 95295899	19950606
				US 9365370	19930524

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DIALOG(R)File 654:US PAT.FULL.  
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4291612

Derwent Accession: 2000-282241

Utility

CERTIFICATE OF CORRECTION

C/ Humanized anti-CD11a antibodies; IMMUNOGLOBULIN WHICH BINDS MAMMALIAN  
PEPTIDE DOMAIN; PREVENTING ADHESION TO HUMAN EPIDERMAL KERATINOCYTES  
EXPRESSING CELLULAR ADHESION MOLECULES

Inventor: Jardieu, Paula M., San Francisco, CA  
Presta, Leonard G., San Francisco, CA

Assignee: Genentech, Inc. (02), South San Francisco, CA  
Genentech Inc (Code: 07579)

Examiner: Saunders, David (Art Unit: 164)

Assistant Examiner: VanderVegt, F. Pierre

Combined Principal Attorneys: Lee, Wendy M.; Schwartz, Timothy R.

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 6037454	A	20000314	US 97974899	19971120
Priority				US 97974899	19971120
Provisional				US 60-31971	19961127

1/3/15 (Item 15 from file: 654)  
DIALOG(R)File 654:US PAT.FULL.  
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4144400

Derwent Accession: 1995-382847

Utility

CERTIFICATE OF CORRECTION

C/ Methods of inducing T cell unresponsiveness to donor tissue or organ in  
a recipient with GP39 antagonists; ADMINISTERING GP39 ANTAGONIST SELECTED  
FROM ANTI-GP36 ANTIBODIES OR FRAGMENTS, SOLUBLE CD40 AND SOLUBLE CD40  
FUSION PROTEINS

Inventor: Noelle, Randolph J., Cornish, NH  
Durie, Fiona H., Seattle, WA  
Parker, David C., Grafton, MA  
Appel, Michael C., Grafton, MA  
Phillips, Nancy E., Shrewsbury, MA  
Mordes, John P., Newton, MA  
Grenier, Dale L., Hubbardston, MA  
Rossini, Aldo A., Sudbury, MA

Assignee: University of Massachusetts Medical Center (02), Worcester, MA

The Trustees of Dartmouth College (02), Hanover, NH  
 Dartmouth College Trustees of  
 Massachusetts, University of Medical Center (Code: 05682 22237)  
 Examiner: Chan, Christina Y. (Art Unit: 164)  
 Assistant Examiner: Gambel, Phillip  
 Law Firm: Burns, Doane, Swecker & Mathis, LLP

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 5902585	A	19990511	US 97906332	19970805
Division	US 5683693	A		US 94234987	19940425
Priority				US 97906332	19970805
				US 94234987	19940425

1/3/18 (Item 18 from file: 654)  
 DIALOG(R)File 654:US PAT.FULL.  
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3904844  
 Derwent Accession: 1995-382847  
 Utility  
 C/ Method for inducing T cell unresponsiveness to a tissue or organ graft  
 with anti-CD40 ligand antibody or soluble CD40  
 Inventor: Noelle, Randolph J., Cornish, NH  
 Durie, Fiona H., Seattle, WA  
 Parker, David C., Grafton, MA  
 Appel, Michael C., Grafton, MA  
 Phillips, Nancy E., Shrewsbury, MA  
 Mordes, John P., Newton, MA  
 Grenier, Dale L., Hubbardston, MA  
 Rossini, Aldo A., Sudbury, MA  
 Assignee: Trustees of Dartmouth College (02), Hanover, NH  
 University of Massachusetts Medical Center (02), Worcester, MA  
 Dartmouth College Trustees of  
 Massachusetts, University of Medical Center (Code: 05682 22237)  
 Examiner: Feisee, Lila (Art Unit: 186)  
 Assistant Examiner: Gambel, Phillip  
 Law Firm: Burns, Doane, Swecker & Mathis

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 5683693	A	19971104	US 94234987	19940425
Priority				US 94234987	19940425

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1/KWIC/2 (Item 2 from file: 654)  
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#### Summary of the Invention:

...related toxicity and from long-term immunosuppression (e.g.  
 infections and secondary malignancies). In addition,  
**transplantation** of bone marrow cells (BMC) or small **intestine**  
 , which are rich in immunocompetent lymphocytes, frequently is associated  
 with a potential life-threatening complication due to **graft** versus  
 host disease (GVHD...

#### Description of the Invention:

...by co-stimulation results in tolerance. Such tolerizing agents  
 include without limitation CTLA4-Ig, anti-B7.1 or anti-  
**B7.2**, anti-CD28, and antibodies against adhesion molecules  
 such as anti-LFA1, anti-CD44, anti-CD40...reagents included CTL4-Ig  
 fusion protein, and antibodies (or functional fragments thereof) specific

for CD40L, B7.1, B7.2, CD28, LFA1, CD44, ICAM-1, CD25, CD69, and MHC class II molecules. While some these...

...relevant antigens to the T cells (e.g., CTLA4-Ig fusion protein and antibodies to B7.1 and B7.2), and some have the potential to interact with molecules on both cell types (e.g...their presentation of the relevant alloantigens without the participation of co-stimulatory molecules (e.g., B7), a mode of antigen presentation known to induce tolerance. In addition, the cytokine profiles observed...

1/KWIC/7 (Item 7 from file: 654)  
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#### Abstract:

...organ. The methods of the invention can be used to induce T cell tolerance to **transplants** such as liver, kidney, heart, lung, skin, muscle, neuronal tissue, stomach and **intestine**. A method for treating diabetes comprising administering to a subject allogeneic or xenogeneic cells expressing...

#### Summary of the Invention:

...a ligand on B cells or other APCs. Ligands for CD28 include members of the B7 family of B lymphocyte activation antigens such as B7-1 and/or B7-2 (Freedman. A. S. et al. (1987) J. Immunol. 137, 3260-3267; Freeman, G. J. et...

...366, 76-79; Freeman, G. J. et al. (1993) J. Exp. Med. 178, 2185-2192). B7-1 and B7-2 are also ligands for another molecule, CTLA4, present on the surface of activated T cells...of the current invention can be used, for example, to induce T cell tolerance to **transplanted** tissue or organs such as liver, kidney, heart, lung, skin, muscle, neuronal tissue, stomach and **intestines**. In one embodiment, the **transplanted** tissue comprises pancreatic islets. Accordingly, the invention provides a method for treating diabetes comprising administering...

#### Description of the Invention:

...may prevent the induction of costimulatory molecules on the allogeneic or xenogeneic cell, (e.g. B7 family molecules on a B cell), so that the cell delivers only an antigenic signal...may lack expression of or express only low levels of costimulatory molecules such as the B7 family of proteins (e.g., B7-1 and B7-2). Expression of costimulatory molecules on potential allogeneic or xenogeneic cells to be used in the...be distinguished from activated B cells by assaying for expression of costimulatory molecules, such as B7-1 and/or B7-2, on the surface of activated B cells by standard techniques (e.g. immunofluorescence...The methods can be used to induce T cell tolerance in a recipient of a **graft** of a tissue or organ such as pancreatic islets, liver, kidney, heart, lung, skin, muscle, neuronal tissue, stomach and **intestines**. Thus, the methods of the invention can be applied in treatments of diseases or conditions which entail tissue or organ **transplantation** (e.g., liver transplantation to treat hypercholesterolemia, transplantation of muscle cells to treat muscular dystrophy...

1/KWIC/8 (Item 8 from file: 654)  
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#### Description of the Drawings:

...FIG. 12 shows PCR analysis mRNA expression of B7-1, B7-2 and OX-2 in various hepatic NPMC cell fractions...

...a graph showing that anti-OX-2 reverses inhibition by NPC. The effect of anti-B7-1, anti-B7-2 and anti-OX-2

#### Description of the Invention:

...UC10-4F10-11) were obtained from Drs. C. June and J. Bluestone respectively, while anti-B7-1, anti-B7-2 were obtained from Dr. G. Powers. High titres of all 4 of the latter antibodies...and FITC anti-rat IgG, anti-OX-2 and PE anti-mouse IgG, FITC-anti-B7-1 or FITC anti-B7-2. Mean staining with Comparison of mouse OX-2 with known cDNA sequences for B7-1, B7-2, CD28 and CTLA4 was performed using a DNASIS program (version 2.0...Using a DNASIS program the predicted mouse protein sequence has some 51% homology with B7-1 and B7-2, 48% with CD28 and 54% with CTLA4 (unpublished...with anti-CD28/anti-CTLA4 (see FIG. 6), or, in studies not shown, using anti-B7-1 or anti-B7-2. Again infusion of the IgG1 isotype control Mab (clone 107.3) did not alter the...was some 50% homology of the predicted protein sequence of murine OX-2 with murine B7-1, B7-2, CD28 and CTLA4 (Borriello et al., 1997), antibodies to the latter molecules did not reverse...6A2, ATCC; biotinylated XMGI.2); anti- IL-10 UES5-2A5; biotinylated SXC-1); PE anti-B7-1/B7-2 (Cedarlane Labs, Hormby, Ontario, Canada...at -70[degree(s)] C. until use in PCR reactions with primers for murine GAPDH, B7-1, B7-2 or OX-2. The sense (S) and antisense (AS) primers were synthesized by the Biotechnology... B7-1 Sense: 5'CCTTGCCGTTACAACCTCTCC3' (SEQ.ID.NO.:12...

...B7-1Antisense: 5'CGGAAGCAAAGCAGGTAATC3' (SEQ.ID.NO.:13...

...B7-2 Sense: 5'TCTCAGATGCTGTTTCCGTG3' (SEQ.ID.NO.:14B7-2 Antisense: 5'GGTTCAGTGAAGTTGGCGAT3' (SEQ.ID.NO.:15...FIG. 11 were tested as follows. Firstly, cells were stained with FITC-labeled Mabs to B7-1, B7-2, NLDC145 and rat anti-mouse OX-2 (M3B5) with FITC anti-rat IgG as second...

...mRNA extracted from the different cell samples were assayed by PCR for expression of GAPDH, B7-1, B7-2 and OX-2. Data are shown in FIGS. 11 (pooled from 3 separate studies) and...FIG. 12 shows PCR detection of B7-1, B7-2 and OX-2 in hepatic NPMC. It is a PCR analysis for mRNA expression of OX-2, B7-1 and B7-2 in various hepatic NPC cell fractions isolated from Flt3L treated mice (see FIG. 11). Data...OX-2 in the cells harvested from Flt3L treated mice, when compared with cells expressing B7-1 and/or B7-2. In general expression of OX-2 and B7-2 occurred in equivalent subpopulations. Faster-sedimenting cells (Fx 3 and 4 in FIG. 11), while staining for NLDC145, were positive by fluorescence mainly for B7-1, not B7-2 or OX-2. Similar conclusions were reached both by FACS analysis of cell populations (FIG...was found that optimal direct stimulation (or proliferation and IL-2 production) was seen from B7-1 expressing cells (Fxs 3 and 4 in panel A) of FIG. 13), while only OX...FIG. 16 is a bar graph showing the effect of anti B7-1; B7-2; or OX-2 on primary allostimulation. It shows that anti-OX-2 Mab ...17). Subsets of these cultures contained in addition either 5 [mu]g/ml of anti-B7-1, anti-B7-2 or anti-OX-2. Supernatants from responder cells stimulated in the presence of DC only...

...Addition of anti-B7-1 or anti-B7-2 to DC stimulated spleen cultures led to inhibition of cytokine production (FIG. 16), while in...within a slow-sedimenting (small size) NLDC145[sup]+ cell population expressing preferentially both cell surface B7-2 and OX-2 (see FIGS. 11 and 12). When it was investigated whether this same...



...function, fresh spleen cells were stimulated with DC alone or in the presence of anti-B7-1, anti-B7-2 or anti-OX-2.

Note that other studies (data not shown) have confirmed that even...

...derived DC used contains small numbers of OX-2<sup>[sup]</sup>+ cells

(RMG-unpublished). Unlike anti-B7-1 and anti-B7-2

which decreased cytokine production, a result in keeping with the hypothesized role for these as...cytokine which might modify development/maturation of DC into a population expressing increased amounts of B7-2 and capable of inducing tolerance

(Steinbrink, K. et al. 1997. J. Immunol. 159:4772-4780...

...in the delivery of a tolerizing signal, perhaps in association with alterations in expression of B7-2, Fas etc. It is intriguing that while there is clearly a key role for intra- ...application of immunoadhesins as therapeutic agents. A CTLA4 immunoadhesion, with the capacity to bind both B7-1 and B7-2, has been used to inhibit T cell costimulation and decrease rejection (Larsen, C. P. et...Ke, P. D. Rennert, G. S. Gray, J. G. Gribben, and L. M. Nadler. 1995. B7-1 and B7-2 do not deliver identical costimulatory signals, since B7-2 but not B7-1

preferentially costimulates the initial production of IL4. Immunity. 2:523-532...Fu. 1996b. A role for gamma delta TCR(+) cells in regulation of rejection of small **intestinal** allografts in rats.

**Transplantation.** 62:844-851...P. S. Linsley, and L. A. Turka. 1996.

Costimulatory function and expression of CD40 ligand, **CD80**, and **CD86** in vascularized murine cardiac allograft rejection. Proc.

Natl. Acad. Sci. USA. 93:13967-13972...S. S. Zamvil, A. Sobel, H. L.

Weiner, N. Nabavi, and L. H. Glimcher. 1995. B7-1 and

B7-2 costimulatory molecules activate differentially the

Th1/Th2 developmental pathways: application to autoimmune disease therapy. Cell...R. P. Lowry, and T. C. Pearson. 1994. Regulation of

immunostimulatory function and costimulatory molecule (B7-1

and B7-2) expression on murine dendritic cells. J. Immunol.

152:52085219...Lenschow, D. J., T. L. Walunas, and J. A. Bluestone. 1996.

CD28/B7 system of T cell costimulation. Annu. Rev. Immunol.

14:233-258...

1/KWIC/9 (Item 9 from file: 654)

DIALOG(R)File 654:(c) FORMAT ONLY 2002 THE DIALOG CORP. All rts. reserv.

#### Summary of the Invention:

...blocker, of the CD40 ligand-CD40 interaction (optionally, an inhibitor or blocker of the CD28-B7 interaction can also be administered...In embodiments wherein the CD28-B7 interaction is inhibited, it can be inhibited by administering a soluble ligand or receptor or antibody for the CD28 or B7, e.g., a soluble CTLA4, e.g., a CTLA4 fusion protein, e.g., a CTLA4 immunoglobulin fusion, e.g., a CTLA4/Ig. Preferably, the inhibitor binds B7. In preferred embodiments anti-B7-1 and/or anti-B7-2 antibodies are administered...

...an anti-CD40L antibody is administered prior to administration of a blocker of the CD28/B7 interaction, e.g., CTLA4/Ig. The CD40/CD40L blocker can be administered on the day donor tissue is introduced and the CD28/B7 blocker administered 2, 3, 4, 5 or more days later...

recipient, a blocker of the CD40 ligand-CD40 interaction (optionally, a blocker of the CD28-B7 interaction can also be administered...lung, or other body parts, such as bone or skeletal matrix, tissue, such as skin, **intestines**, endocrine glands, or progenitor stem cells of various types, are all examples of **grafts**.

"

Description of the Invention:

...administration of inhibitors of the CD40 ligand-CD40 (and optionally an inhibitor of the CD28-B7 interaction) and transplantation of tolerance-inducing stem cells, e.g., bone marrow stem cells. The...or more loci at each of class I and class II. In preferred embodiments: the **graft** includes tissue from the digestive tract or gut, e.g., tissue from the stomach, or bowel tissue, e. g., small **intestine**, large **intestine**, or colon; the **graft** replaces a portion of the recipient's digestive system e.g., all or part of...Blockers of the CD40 ligand-CD40 interaction (and optionally the CD28-B7 interaction) (or both) can be administered repeatedly. E.g., blockers can be administered one, two...CD40-CD40L blockers can be administered prior to CD28-B7 blockers, if CD2-B7 blockers are used. They can also be administered at the same time or after CD2-B7 blockers, if CD2-B7 blockers are used...

2. The method of claim 1, further comprising administering an inhibitor of the CD28-B7 interaction...

...5. The method of claim 2, wherein the CD28-B7 interaction is inhibited by administering a soluble ligand or receptor or antibody for the CD28 or B7.

...

...the CD40/CD40L interaction is administered prior to administration of a blocker of the CD28/B7 interaction

1/KWIC/13

(Item 13 from file: 654)

DIALOG(R)File 654:(c) FORMAT ONLY 2002 THE DIALOG CORP. All rts. reserv.

Summary of the Invention:

...are successful in saving lives and improving the quality of life. The list of successfully **transplanted** tissues includes: kidney,

heart, lung, liver, corneas, pancreas, pancreatic islets of Langerhans, **intestines**, brain tissue, liver, spleen, thymus, lymph nodes, bone marrow, skin, and bones. Combinations of tissue have also been

**transplanted**; for example, heart-lung **transplants**, pancreas-kidney **transplants**, and pancreas-kidney-intestinal

**transplants**.

...269, and D. Shafer et al., "Prevention of Graft-versus-host Disease Following Small Bowel **Transplantation** with Polyclonal and Monoclonal Antilymphocyte Serum", **TRANSPLANTATION**, Vol. 52, teaches that GvHD by lymphocytes from the **intestine** is a major problem after **intestinal transplants**. They disclose that GvHD can be prevented by treating the donor with antilymphocyte serum (ALS...

...including endothelium, macrophages, dendritic cells, plasma cells, etc. Although the risk of GvHD from the **intestinal transplant** is reduced, the **graft** is still at risk for rejection and is still immune deficient and at risk for...specific regulatory cells and factors, including suppressor cells, veto cells, antigen presenting cells defective for **B7** and related surface molecules, cells producing anti-idiotypic antibodies and anti-idiotypic antibodies for the...

...method for generating regulatory cells including suppressor cells, veto cells, antigen presenting cells defective for **B7** and related surface molecules, cells producing anti-idiotypic antibodies and anti-idiotypic antibodies responsible for...

Description of the Invention:

...such as suppressor cells, veto cells and antigen presenting cells deficient in surface expression of **B7** or related molecules. [sup]1

...Footnote: [sup]1 B7 is a ligand for T cell surface antigen CD28 that is expressed by antigen presenting...

...monocytes, and dendritic cells. Antigen presentation by MHC class II molecules on cells that express B7 induces optimal T cell proliferation and cytokine production, but antigen presentation by MHC class II molecules in the absence of B7/CD28 binding results in tolerance to the antigen. Gimmi, et al., PROC. NATL. ACAD. SCI...Cats and dogs have been commonly used as large animal models for **transplantation**, including bone marrow, lung, **intestine**, and bone **transplants** (Ladiges, et al., LAB. ANIM. SCI., 40:11-15, 1990; Henry, et al., AM. J...be conducted to establish chimerism and to rule out GvHD and immune reactions to the **graft** tissue. Immunopathology studies may be performed on biopsies of the skin, the liver, the **intestines**, the bronchial mucosa, the thymus, the lymph nodes, the spleen, and/or other tissues from the intended **graft**. These target tissues are stained and evaluated for cellular injury indicative of GvHD or organ...cells, cells producing anti-idiotypic antibodies, veto cells, and/or antigen presenting cells deficient in B7 or similar molecules. Such cells may be obtained from a surrogate animal treated as taught...**Transplant** organs or tissues having an immune component (for example, the lungs and **intestines**) normally go through a phase of immune deficiency between the time when the donor leukocytes...against infections, and the loss of the monocytes, macrophages, and dendritic cells may leave the **graft**, especially lung and **intestinal grafts**, susceptible to opportunistic infection...

...The intestines are usually regarded as a digestive organ. However, the **intestinal** tract is also the largest lymphoid organ in the body. GvHD resulting from the resident lymphocytes attacking the organ **graft** recipient poses a major problem following **transplantation** of **intestines**. The GvHD resulting from the resident lymphocytes attacking the organ **graft** recipient has also been reported after liver **transplantation**, and is potentially a problem with lung transplants...

1/KWIC/14 (Item 14 from file: 654)  
DIALOG(R)File 654:(c) FORMAT ONLY 2002 THE DIALOG CORP. All rts. reserv.

#### Description of the Invention:

...be used to replace damaged portions of esophagus, blood vessels, or bile duct. The skin **grafts** can be used not only for burns, but also as a dressing to damaged **intestine** or to close certain defects such as diaphragmatic hernia. The **graft** is derived from any mammalian source, including human, whether from cadavers or living donors. Preferably...Biol. 8: 2159-2165 (1988)); the c-myc tag and the 8F9, 3C7, 6E10, G4, B7 and 9E10 antibodies thereto (Evan et al., Mol. Cell. Biol. 5(12):3610-3616 (1985...)

1/KWIC/15 (Item 15 from file: 654)  
DIALOG(R)File 654:(c) FORMAT ONLY 2002 THE DIALOG CORP. All rts. reserv.

#### Abstract:

...organ. The methods of the invention can be used to induce T cell tolerance to **transplants** such as liver, kidney, heart, lung, skin, muscle, neuronal tissue, stomach and **intestine**. A method for treating diabetes comprising administering to a subject allogeneic or xenogeneic cells expressing...

#### Summary of the Invention:

...a ligand on B cells or other APCs. Ligands for CD28 include members of the B7 family of B lymphocyte activation antigens. such as

B7-1 and/or B7-2 (Freedman, A. S. et al. (1987)  
J. Immunol. 137, 3260-3267; Freeman, G. J. et...

...366, 76-79; Freeman, G. J. et al. (1993) J. Exp. Med. 178, 2185-2192).  
B7-1 and B7-2 are also ligands for another molecule, CTLA4, present on the surface of activated T cells...of the current invention can be used, for example, to induce T cell tolerance to **transplanted** tissue or organs such as liver, kidney, heart, lung, skin, muscle, neuronal tissue, stomach and **intestines**. In one embodiment, the **transplanted** tissue comprises pancreatic islets. Accordingly, the invention provides a method for treating diabetes comprising administering...

#### Description of the Invention:

...may prevent the induction of costimulatory molecules on the allogeneic or xenogeneic cell, (e.g. B7 family molecules on a B cell), so that the cell delivers only an antigenic signal...may lack expression of or express only low levels of costimulatory molecules such as the B7 family of proteins (e.g., B7-1 and B7-2). Expression of costimulatory molecules on potential allogeneic or xenogeneic cells to be used in the...be distinguished from activated B cells by assaying for expression of costimulatory molecules, such as B7-1 and/or B7-2, on the surface of activated B cells by standard techniques (e.g. immunofluorescence...The methods can be used to induce T cell tolerance in a recipient of a **graft** of a tissue or organ such as pancreatic islets, liver, kidney, heart, lung, skin, muscle, neuronal tissue, stomach and **intestines**. Thus, the methods of the invention can be applied in treatments of diseases or conditions which entail tissue or organ **transplantation** (e.g., liver transplantation to treat hypercholesterolemia, transplantation of muscle cells to treat muscular dystrophy...

1/KWIC/18 (Item 18 from file: 654)  
DIALOG(R) File 654:(c) FORMAT ONLY 2002 THE DIALOG CORP. All rts. reserv.

#### Abstract:

...organ. The methods of the invention can be used to induce T cell unresponsiveness to **transplants** such as liver, kidney, heart, lung, skin, muscle, neuronal tissue, stomach and **intestine**. A method for treating diabetes comprising administering to a subject allogeneic or xenogeneic cells expressing...

#### Summary of the Invention:

...a ligand on B cells or other APCs. Ligands for CD28 include members of the B7 family of B lymphocyte activation antigens, such as B7-1 and/or B7-2 (Freedman, A. S. et al. (1987)  
J. Immunol. 137, 3260-3267; Freeman, G. J. et...

...366, 76-79; Freeman, G. J. et al. (1993) J. Exp. Med. 178, 2185-2192).  
B7-1 and B7-2 are also ligands for another molecule, CTLA4, present on the surface of activated T cells...of the current invention can be used, for example, to induce T cell tolerance to **transplanted** tissue or organs such as liver, kidney, heart, lung, skin, muscle, neuronal tissue, stomach and **intestines**. In one embodiment, the **transplanted** tissue comprises pancreatic islets. Accordingly, the invention provides a method for treating diabetes comprising administering...

#### Description of the Invention:

...may prevent the induction of costimulatory molecules on the allogeneic or xenogeneic cell, (e.g. B7 family molecules on a B cell), so that the cell delivers only an antigenic signal...may lack expression of or express only low levels of costimulatory molecules such

as the B7 family of proteins (e.g., B7-1 and B7-2). Expression of costimulatory molecules on potential allogeneic or xenogeneic cells to be used in the...

...be distinguished from activated B cells by assaying for expression of costimulatory molecules, such as B7-1 and/or B7-2, on the surface of activated B cells by standard techniques (e.g. immunofluorescence...). The methods can be used to induce T cell tolerance in a recipient of a **graft** of a tissue or organ such as pancreatic islets, liver, kidney, heart, lung, skin, muscle, neuronal tissue, stomach and **intestines**. Thus, the methods of the invention can be applied in treatments of diseases or conditions which entail tissue or organ **transplantation** (e.g., liver transplantation to treat hypercholesterolemia, transplantation of muscle cells to treat muscular dystrophy...  
?

Set	Items	Description
S1	26	(CD80 OR CD86 OR B7 OR B7(W)1 OR B7(W)2) AND (INTESTIN?) (2-0N) (TRANSPLANT? OR GRAFT?)
?		

SYSTEM:OS - DIALOG OneSearch

File 5:Biosis Previews(R) 1969-2002/Sep W5  
(c) 2002 BIOSIS

\*File 5: Alert feature enhanced for multiple files, duplicates removal, customized scheduling. See HELP ALERT.

File 73:EMBASE 1974-2002/Sep W5  
(c) 2002 Elsevier Science B.V.

\*File 73: Alert feature enhanced for multiple files, duplicates removal, customized scheduling. See HELP ALERT.

File 155:MEDLINE(R) 1966-2002/Sep W5

\*File 155: Alert feature enhanced for multiple files, duplicates removal, customized scheduling. See HELP ALERT.

File 399:CA SEARCH(R) 1967-2002/UD=13713  
(c) 2002 American Chemical Society

\*File 399: Use is subject to the terms of your user/customer agreement.  
Alert feature enhanced for multiple files, etc. See HELP ALERT.

Set Items Description

? s (b7 or b7(w)1 or B7(w)2 or cd80 or cd86) and (intestin?)(20n)(graft? or transplant?)

Processing

Processing

Processing

16235	B7
16235	B7
8680318	1
4900	B7(W)1
16235	B7
8393421	2
4231	B7(W)2
7942	CD80
6204	CD86
776555	INTESTIN?
493662	GRAFT?
1352163	TRANSPLANT?
11754	INTESTIN?(20N)(GRAFT? OR TRANSPLANT?)
S1 34	(B7 OR B7(W)1 OR B7(W)2 OR CD80 OR CD86) AND (INTESTIN?)(20N)(GRAFT? OR TRANSPLANT?)

? rd s1

...completed examining records

S2 20 RD S1 (unique items)

? t s2/7/all

2/7/1 (Item 1 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

(c) 2002 BIOSIS. All rts. reserv.

13167549 BIOSIS NO.: 200100374698

**CD80/86 and Th1 cytokine expression in intestinal graft**  
following reperfusion and endotoxemia.

AUTHOR: Wada M; Amae S; Ishii T; Sano N; Sasaki H; Nio M; Hayashi Y; Ohi R  
(a)

AUTHOR ADDRESS: (a)Department of Pediatric Surgery, Tohoku University  
School of Medicine, 1-1 Seiryō-machi, Aoba-ku, Sendai, 980-8574\*\*Japan

JOURNAL: Transplantation Proceedings 33 (1-2):p345-346 February-March,  
2001

MEDIUM: print

CONFERENCE/MEETING: XVIII International Congress of the Transplantation  
Society Rome, Italy August 29-September 01, 2000

SPONSOR: Transplantation Society

ISSN: 0041-1345

RECORD TYPE: Citation

LANGUAGE: English  
SUMMARY LANGUAGE: English

2/7/2 (Item 2 from file: 5)  
DIALOG(R) File 5: Biosis Previews(R)  
(c) 2002 BIOSIS. All rts. reserv.

13142026 BIOSIS NO.: 200100349175  
CD8 T cell-mediated rejection of intestinal allografts is resistant to inhibition of the CD40/CD154 costimulatory pathway.  
AUTHOR: Guo Zhong; Meng Lingzhong; Kim Oliver; Wang Jun; Hart John; He Gang ; Alegre Maria-Luisa; Thistlethwaite J Richard Jr; Pearson Thomas C; Larsen Christian P; Newell Kenneth A(a)  
AUTHOR ADDRESS: (a) Department of Surgery, University of Chicago, 5841 South Maryland Avenue, Chicago, IL, 60637: newell@surgery.bsd.uchicago.edu\*\*USA  
JOURNAL: Transplantation (Baltimore) 71 (9):p1351-1354 May 15, 2001  
MEDIUM: print  
ISSN: 0041-1337  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English  
SUMMARY LANGUAGE: English

ABSTRACT: Background: Disruption of the CD40/CD154 pathway inhibits rejection in numerous models. The importance of this pathway on **intestinal** allograft rejection was examined in this study. Methods: **Intestinal grafts** from B6C3F1 mice **transplanted** into C57BL/6 recipients were assessed histologically for rejection. Results: The monoclonal antibody to CD154, MR1, failed to inhibit rejection in wild-type mice. Similarly, CD154-/- recipient mice rejected intestinal allografts. MR1 did inhibit early rejection in CD8-/- mice, but had no effect in CD4-/- recipients. All MR1-treated CD8-/- recipients eventually developed rejection. No benefit was observed when blockade of the CD40/CD154 pathway by MR1 was combined with blockade of the CD28/B7 pathway by mCTLA4Ig. Conclusions: These data suggest that CD4+ T cells mediating intestinal allograft rejection may be more dependent upon the CD40/CD154 pathway than CD8+ T cells. This finding highlights the importance of identifying agents that suppress CD8+ T cell-mediated rejection.

2/7/3 (Item 1 from file: 73)  
DIALOG(R) File 73: EMBASE  
(c) 2002 Elsevier Science B.V. All rts. reserv.

11618690 EMBASE No: 2002190464  
Expression of the co-stimulatory molecule **CD80 (B7-1)** in a porcine **intestinal graft**  
Wada M.; Amae S.; Sano N.; Ishii T.; Sasaki H.; Nishi K.; Nio M.; Hiyashi Y.; Ohi R.  
Dr. R. Ohi, Department of Pediatric Surgery, Tohoku University School of Medicine, 1-1 Seiryomachi, Aoba-ku, Sendai 980-8574 Japan  
Transplantation Proceedings ( TRANSPLANT. PROC. ) (United States) 2002 , 34/3 (1042-1044)  
CODEN: TRPPA ISSN: 0041-1345  
PUBLISHER ITEM IDENTIFIER: S0041134502  
DOCUMENT TYPE: Journal ; Conference Paper  
LANGUAGE: ENGLISH  
NUMBER OF REFERENCES: 5

2/7/4 (Item 2 from file: 73)  
DIALOG(R) File 73: EMBASE



(c) 2002 Elsevier Science B.V. All rts. reserv.

11366232 EMBASE No: 2001380446

Cutting edge: Membrane lymphotoxin regulates CD8SUP+ T cell-mediated intestinal allograft rejection

Guo Z.; Wang J.; Meng L.; Wu Q.; Kim O.; Hart J.; He G.; Zhou P.;

Thistlethwaite J.R. Jr.; Alegre M.-L.; Fu Y.-X.; Newell K.A.

Dr. K.A. Newell, Department of Surgery, Emory University, WMB 5105, 1639  
Pierce Drive, Atlanta, GA 30322 United States

AUTHOR EMAIL: kenneth.newell@emory.org

Journal of Immunology ( J. IMMUNOL. ) (United States) 01 NOV 2001,  
167/9 (4796-4800)

CODEN: JOIMA ISSN: 0022-1767

DOCUMENT TYPE: Journal ; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 27

Blocking the CD28/B7 and/or CD154/CD40 costimulatory pathways promotes long-term allograft survival in many transplant models where CD4SUP+ T cells are necessary for rejection. When CD8SUP+ T cells are sufficient to mediate rejection, these approaches fail, resulting in costimulation blockade-resistant rejection. To address this problem we examined the role of lymphotoxin-related molecules in CD8SUP+ T cell-mediated rejection of murine intestinal allografts. Targeting membrane lymphotoxin by means of a fusion protein, mAb, or genetic mutation inhibited rejection of intestinal allografts by CD8SUP+ T cells. This effect was associated with decreased monokine induced by IFN-gamma (Mig) and secondary lymphoid chemokine (SLC) gene expression within allografts and spleens respectively. Blocking membrane lymphotoxin did not inhibit rejection mediated by CD4SUP+ T cells. Combining disruption of membrane lymphotoxin and treatment with CTLA4-Ig inhibited rejection in wild-type mice. These data demonstrate that membrane lymphotoxin is an important regulatory molecule for CD8SUP+ T cells mediating rejection and suggest a strategy to avoid costimulation blockade-resistant rejection.

2/7/5 (Item 3 from file: 73)

DIALOG(R) File 73:EMBASE

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10637567 EMBASE No: 2000101054

Blockade of the B7-CD28 pathway by CTLA4-Ig counteracts rejection and prolongs survival in small bowel transplantation

Kurlberg G.; Haglund E.; Schon K.; Tornqvist H.; Lycke N.

G. Kurlberg, Department of Surgery, Sahlgrenska Univ. Hospital/Ostra,  
SE-416 85 Goteborg Sweden

Scandinavian Journal of Immunology ( SCAND. J. IMMUNOL. ) (United Kingdom)  
) 2000, 51/3 (224-230)

CODEN: SJIMA ISSN: 0300-9475

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 32

Allograft rejection involves T-cell activation, requiring T-cell receptor interactions with major histocompatibility complex (MHC) molecules and costimulatory signals delivered through the B7-CD28 pathway. We evaluated the effect of blocking this pathway on graft rejection and survival, in a rat experimental model of small bowel transplantation. Heterotopic small bowel transplantation was performed between PVG donor rats and DA recipient rats. The recipient animals were treated with CTLA4-Ig or irrelevant immunoglobulin (Ig)G as control and followed for 18, 30 or 90 days. The survival rate and degree of inflammation and accumulation of CD4sup + T cells and macrophages were determined in the transplanted bowels. We found that administration of CTLA4- Ig

significantly improved the survival rate compared to control rats: after 30 days 73% of the treated rats had survived and at 90 days 5/8 rats were still living, whereas in the control group only 2/8 rats had survived. The grafts showed preserved mucosal structure with only a mild degree of subacute inflammation and the accumulation of CD4sup +T cells and macrophages was noticeably reduced in treated animals as compared to control rats. Necrosis was extensive in control rats, whereas CTLA4-Ig treated animals had grafts with at least some preserved villus morphology and no necrotic tissue. Although small bowel transplantation has proven exceptionally difficult, in this study we have shown that CTLA4-Ig treatment may provide a promising strategy to prevent rejection and induce long term tolerance and graft survival.

2/7/6 (Item 4 from file: 73)  
DIALOG(R) File 73:EMBASE  
(c) 2002 Elsevier Science B.V. All rts. reserv.

07807817 EMBASE No: 1999297285  
Cutting edge: Blockade of the CD28/B7 costimulatory pathway inhibits intestinal allograft rejection mediated by CD4sup + but not CD8sup + T cells  
Newell K.A.; He G.; Guo Z.; Kim O.; Szot G.L.; Rulifson I.; Zhou P.; Hart J.; Thistlethwaite J.R.; Bluestone J.A.  
Dr. K.A. Newell, Department of Surgery, MC 5026, University of Chicago, 5841 South Maryland Avenue, Chicago, IL 60637 United States  
AUTHOR EMAIL: newell@surgery.bsd.uchicago.edu  
Journal of Immunology ( J. IMMUNOL. ) (United States) 01 SEP 1999, 163/5 (2358-2362)  
CODEN: JOIMA ISSN: 0022-1767  
DOCUMENT TYPE: Journal; Article  
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH  
NUMBER OF REFERENCES: 17

The effect of blocking the CD28/B7 costimulatory pathway on **intestinal** allograft rejection was examined in mice. Murine CTLA4Ig failed to prevent the rejection of allografts **transplanted** into wild-type or CD4 knockout (KO) mice but did inhibit allograft rejection by CD8 KO recipients. This effect was associated with decreased intragraft mRNA for IFN-gamma and TNF-alpha and increased mRNA for IL-4 and IL-5. This altered pattern of cytokine production was not observed in allografts from murine CTLA4Ig-treated CD4 KO mice. These data demonstrate that blockade of the CD28/B7 pathway has different effects on intestinal allograft rejection mediated by CD4sup + and CD8sup + T cells and suggest that T cell subsets have different costimulatory requirements in vivo. The results also suggest that the inhibition of CD4sup + T cell-mediated allograft rejection by CTLA4Ig may be related to down-regulation of Th1 cytokines and/or up-regulation of Th2 cytokines.

2/7/7 (Item 5 from file: 73)  
DIALOG(R) File 73:EMBASE  
(c) 2002 Elsevier Science B.V. All rts. reserv.

07614757 EMBASE No: 1999088574  
CTLA4IgG treatment induces long-term acceptance of rat small bowel allografts  
Tarumi K.; Murakami M.; Yagihashi A.; Nakagawa I.; Hirata K.; Uede T.  
Dr. T. Uede, Section of Immunopathogenesis, Institute of Immunological Science, Hokkaido University, Kita-15, Nishi 7, Kita-ku, Sapporo 060-0815 Japan  
Transplantation ( TRANSPLANTATION ) (United States) 27 FEB 1999, 67/4 (520-525)  
CODEN: TRPLA ISSN: 0041-1337

DOCUMENT TYPE: Journal; Article  
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH  
NUMBER OF REFERENCES: 31

Background. CTLA4 immunoglobulin (Ig)G that binds to B7 effectively inhibits the signaling of CD28/CTLA4-B7 pathway and induces antigen specific T cell unresponsiveness in vitro and in vivo. Using CTLA4IgG, we examined induction of long-term graft survival and the mechanism of maintenance of tolerance in rat allogeneic small bowel transplantation. Methods. Small bowels of Brown-Norway rats (RT1(n)) were heterotopically transplanted into Lewis rats (RT1sup 1). Recipients were treated with an i.p. injection of either CTLA4IgG or control IgG for 7 days. Results. Long-term survival was observed in rats treated with CTLA4IgG, whereas control rats died within 16 days after transplantation. To examine whether a tolerant state was established in long-term survival rats, secondary transplantation was performed using small bowels of Brown-Norway rats or ACI (RT1sup b) rats. It was demonstrated that small bowels of Brown-Norway rats were accepted; however, those of ACI rats were rejected within 10 days. Serum concentrations of interleukin (IL)-4 were maintained at >50 mug/ml for 7 days after transplantation in rats treated with CTLA4IgG but <15 mug/ml in control recipients. Serum IFN-gamma in CTLA4IgG-treated recipients increased after transplantation and was not distinguishable from that of control recipients during the first 7 days after transplantation. Conclusion. We demonstrated that CTLA4IgG treatment alone for 7 days induced a long-term donor specific tolerance rat allogeneic small bowel transplantation. The induction of long-term acceptance of small bowel allografts by CTLA4IgG is not caused by simply the shift of anti-alloimmune responses from Th1 to Th2 cytokine production.

2/7/8 (Item 6 from file: 73)  
DIALOG(R)File 73:EMBASE  
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07428703 EMBASE No: 1998337926  
Prolongation of rat small bowel allograft survival of CTLA-4 IG  
Tarumi K.; Yagihashi A.; Murakami M.; Uede T.; Hirata K.  
Dr. K. Tarumi, First Department of Surgery, Sapporo Med. Univ. Sch. of  
Medicine, South 1 West 16, Sapporo 060 Japan  
Transplantation Proceedings ( TRANSPLANT. PROC. ) (United States) 1998,  
30/6 (2596-2599)  
CODEN: TRPPA ISSN: 0041-1345  
PUBLISHER ITEM IDENTIFIER: S0041134598007441  
DOCUMENT TYPE: Journal; Conference Paper  
LANGUAGE: ENGLISH  
NUMBER OF REFERENCES: 16

2/7/9 (Item 7 from file: 73)  
DIALOG(R)File 73:EMBASE  
(c) 2002 Elsevier Science B.V. All rts. reserv.

07023864 EMBASE No: 1997320565  
Survival of rat small bowel allografts treated with allotrap 07(R)  
Tice D.G.; Bruch D.; Buelow R.; Squiers E.C.  
Dr. D.G. Tice, Department of Surgery, New York State Univ. Hlth. Sci.  
Ctr., Syracuse, NY 13210 United States  
Journal of Surgical Research ( J. SURG. RES. ) (United States) 1997,  
72/1 (78-83)  
CODEN: JSGRA ISSN: 0022-4804  
DOCUMENT TYPE: Journal; Article  
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH  
NUMBER OF REFERENCES: 18

Previous reports from other investigators demonstrate prolongation of allogeneic heart graft survival and decrease in CTL responses in rats treated with a small synthetic peptide corresponding to residues 75-84 of the human HLA-B7-01 molecule (Allotrap 07(R)). We wished to determine the efficacy of these peptides in the highly immunogenic ACI > LEW and LEW > ACI small bowel transplant models. Animals were divided into treatment groups: I, none; II, Allotrap (20 mg/kg/day on Days 0-4); III, cyclosporine (CsA; 10 mg/kg/day on Days 0-4); IV, Allotrap + CsA (as in groups II and III); V, Allotrap (40 mg/kg/day every other day on Days -19 to 4); VI, Allotrap + CsA (as in groups III and V); VII, Allotrap + CsA (as in groups III and V, with Allotrap administered intragraft Days 0-4). The animals were sacrificed at the time of graft rejection (defined by dusky, necrotic stoma and increased stomal output). Peripheral blood, spleen, native bowel, and allograft intraepithelial and lamina propria lymphocytes were harvested and mixed lymphocyte culture (MLC) reactivity against self, donor, and third-party splenocytes was assessed. Statistical analysis was performed by ANOVA with Dunnett's t for multiple comparisons against a control as a post hoc test. We found a very slight, but significant prolongation of graft survival in with treatment protocol V for both strain combinations. In addition, MLC response of splenocytes to donor antigen was decreased with combined CsA and Allotrap, but not with Allotrap alone. We conclude that Allotrap decreases response to alloantigens, and slightly, but significantly prolongs graft survival in the highly immunogenic small bowel transplant model.

2/7/10 (Item 8 from file: 73)  
DIALOG(R)File 73:EMBASE  
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06820692 EMBASE No: 1997103185

Treatment with an HLA-peptide and cyclosporine a prolongs rat small bowel allograft survival

Willettts I.E.; Tam P.K.H.; Morris P.J.; Dallman M.J.

P.K.H. Tam, Division of Paediatric Surgery, Department of Surgery,

University of Hong Kong, Hong Kong Hong Kong

Journal of Pediatric Surgery ( J. PEDIATR. SURG. ) (United States) 1997

, 32/3 (469-472)

CODEN: JPDSA ISSN: 0022-3468

DOCUMENT TYPE: Journal; Conference Paper

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 23

IC option is not available in file(s): 399

1/KWIC/19 (Item 6 from file: 155)  
DIALOG(R) File 155:

Adenovirus-mediated CTLA4-IgG gene therapy in orthotopic small  
**intestinal transplantation** in rats.

Descriptors: Antigen, CD28--drug effects--DE; \*Antigen, CD80  
--drug effects--DE; \*Antigen, Differentiation--therapeutic use--TU; \*Gene  
Therapy--methods--MT; \*Genetic Vectors--therapeutic use--TU; \*Immunoglobulin  
G--therapeutic use--TU; \*Immunosuppressive Agents--therapeutic use--TU; \*  
**Intestine, Small--transplantation--TR**

Chemical Name: Antigen, CD28; Antigen, CD80; Antigen,  
Differentiation; CTLA-4; Genetic Vectors; Immunoglobulin G;  
Immunosuppressive Agents

1/KWIC/20 (Item 7 from file: 155)  
DIALOG(R) File 155:

; Adoptive Transfer; Antigen-Presenting Cells--immunology--IM; Antigen,  
CD--biosynthesis--BI; Antigen, CD80--biosynthesis--BI; CD4-Positive  
T-Lymphocytes--immunology--IM; Chickens; Down-Regulation--immunology--IM;  
Eating--immunology--IM; Epitopes, T-Lymphocyte--immunology--IM; Freund's  
Adjuvant--pharmacology--PD; **Intestinal** Diseases, Parasitic  
--metabolism--ME; **Intestinal** Mucosa--immunology--IM; Lymph Nodes  
--cytology--CY; Lymph Nodes--immunology--IM; Lymph Nodes--  
**transplantation--TR**; Lymphocyte Transformation; Lymphoid Tissue  
--immunology--IM; Membrane Glycoproteins--biosynthesis--BI; Mesentery; Mice  
; Mice, Inbred...

Chemical Name: Adjuvants, Immunologic; Antigen; Antigen, CD; Antigen,  
CD80; B7-2 protein; Epitopes, T-Lymphocyte; Membrane  
Glycoproteins; Receptors, Antigen, T-Cell; incomplete Freund's adjuvant;  
Ovalbumin...

? t s1/3/19,20

>>>Leading comma in item list

? t s1/3/19,20

1/3/19 (Item 6 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)

11153664 21168315 PMID: 11266771

Adenovirus-mediated CTLA4-IgG gene therapy in orthotopic small  
**intestinal transplantation** in rats.

Echizenya H; Yamashita K; Takehara M; Konishi K; Nomura M; Yanagida N;  
Kitagawa N; Kobayashi T; Furukawa H; Inobe M; Uede T; Todo S

First Department of Surgery, Hokkaido University, School of Medicine,  
Sapporo, Japan.

Transplantation proceedings (United States) Feb-Mar 2001, 33 (1-2)  
p183-4, ISSN 0041-1345 Journal Code: 0243532

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

1/3/20 (Item 7 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)

10959772 20540071 PMID: 11086051

Enteric infection acts as an adjuvant for the response to a model food  
antigen.

Shi H N; Liu H Y; Nagler-Anderson C

Mucosal Immunology Laboratory, Massachusetts General Hospital, and

Harvard Medical School, Charlestown, MA 02129, USA.

Journal of immunology (Baltimore, Md. : 1950) (UNITED STATES) Dec 1  
2000, 165 (11) p6174-82, ISSN 0022-1767 Journal Code: 2985117R  
Contract/Grant No.: DK35506; DK; NIDDK; DK47017; DK; NIDDK  
Document type: Journal Article  
Languages: ENGLISH  
Main Citation Owner: NLM  
Record type: Completed

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B7-2.USPT.	240
B7-2S	0
B7.USPT.	8090
B7S	0
CD80.USPT.	173
CD80S	0
CD86.USPT.	149
CD86S	0
RAPAMYCIN.USPT.	955
((('B7-1' OR 'B7-2' OR B7 OR CD80 OR CD86)SAME (ANTIBOD\$) AND (GRAFT\$ OR TRANSPLANT\$) AND RAPAMYCIN).USPT.	42

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side by side

*DB=USPT; PLUR=YES; OP=ADJ*L2 ('b7-1' or 'b7-2' or b7 or cd80 or cd86)same (antibod\$) and (graft\$ or transplant\$) and rapamycinL1 ('b7-1' or 'b7-2' or b7 or cd80 or cd86)same (antibod\$) and (graft\$ or transplant\$) same (intestine\$)**Hit Count Set Name**  
result set42 L216 L1

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B7-1S	0
B7-2.DWPI,EPAB,JPAB.	42
B7-2S	0
B7.DWPI,EPAB,JPAB.	1482
B7S	0
CD80.DWPI,EPAB,JPAB.	50
CD80S	0
CD86.DWPI,EPAB,JPAB.	63
CD86S	0
ANTIBOD\$	0
((('B7-1' OR 'B7-2' OR B7 OR CD80 OR CD86)SAME (ANTIBOD\$) AND (GRAFT\$ OR TRANSPLANT\$) SAME (INTESTINE\$)).JPAB,EPAB,DWPI.	1

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<u>L3</u>	('b7-1' or 'b7-2' or b7 or cd80 or cd86)same (antibod\$) and (graft\$ or transplant\$) same (intestine\$)	1	<u>L3</u>
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<u>L2</u>	('b7-1' or 'b7-2' or b7 or cd80 or cd86)same (antibod\$) and (graft\$ or transplant\$) and rapamycin	42	<u>L2</u>
<u>L1</u>	('b7-1' or 'b7-2' or b7 or cd80 or cd86)same (antibod\$) and (graft\$ or transplant\$) same (intestine\$)	16	<u>L1</u>

END OF SEARCH HISTORY

From: Gambel, Phillip  
Sent: Saturday, October 05, 2002 9:30 AM  
T : STIC-ILL  
Subject: collins intestine amd 09 / 805801

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please provide the following references to

phillip gambel  
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2/7/16 (Item 5 from file: 155)  
DIALOG(R)File 155:MEDLINE(R)

10395122 99384046 PMID: 10452966

Cutting edge: blockade of the CD28/B7 costimulatory pathway inhibits intestinal allograft rejection mediated by CD4+ but not CD8+ T cells.

Newell K A; He G; Guo Z; Kim O; Szot G L; Rulifson I; Zhou P; Hart J; Thistlethwaite J R; Bluestone J A

Department of Surgery, Committee on Immunology, Ben May Institute for Cancer Research, University of Chicago, IL 60637, USA.  
newell@surgery.bsd.uchicago.edu

Journal of immunology (Baltimore, Md. : 1950) (UNITED STATES) Sep 1 1999, 163 (5) p2358-62, ISSN 0022-1767 Journal Code: 2985117R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The effect of blocking the CD28/B7 costimulatory pathway on intestinal allograft rejection was examined in mice. Murine CTLA4Ig failed to prevent the rejection of allografts transplanted into wild-type or CD4 knockout (KO) mice but did inhibit allograft rejection by CD8 KO recipients. This effect was associated with decreased intragraft mRNA for IFN-gamma and TNF-alpha and increased mRNA for IL-4 and IL-5. This altered pattern of cytokine production was not observed in allografts from murine CTLA4Ig-treated CD4 KO mice. These data demonstrate that blockade of the CD28/B7 pathway has different effects on intestinal allograft rejection mediated by CD4+ and CD8+ T cells and suggest that these T cell subsets have different costimulatory requirements in vivo. The results also suggest that the inhibition of CD4+ T cell-mediated allograft rejection by CTLA4Ig may be related to down-regulation of Th1 cytokines and/or up-regulation of Th2 cytokines.

Record Date Created: 19990914

07614757 EMBASE No: 1999088574

CTLA4IgG treatment induces long-term acceptance of rat small bowel allografts

Tarumi K.; Murakami M.; Yagihashi A.; Nakagawa I.; Hirata K.; Uede T. Dr. T. Uede, Section of Immunopathogenesis, Institute of Immunological Science, Hokkaido University, Kita-15, Nishi 7, Kita-ku, Sapporo 060-0815 Japan

Transplantation ( TRANSPLANTATION ) (United States) 27 FEB 1999, 67/4 (520-525)

CODEN: TRPLA ISSN: 0041-1337

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

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